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DILEMMAS OF LIFE AND DEATH WITH CYANIDE TOXICITY

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ABSTRACT

Cyanide is one of the oldest poisons. Large doses of cyanide prevent cells from using oxygen and eventually these cells die. The heart, respiratory system and central nervous system are most susceptible to cyanide. Cyanide directly stimulates the chemo-receptors of the carotid and aortic bodies that results in hyperpnoea. Cardiac irregularities are often noted, but the heart invariably outlasts the respirations. The central origin of death is due to respiratory arrest. Hydrocyanic acid (HCN), sodium cyanide (NaCN) and potassium cyanide (KCN) or cyanogen are very potent, extremely lethal and most rapidly fatal. Poisoning with hydrocyanic acid is almost always fatal because of the low fatal dose and the rapidity with which it acts.

KEYWORDS: Hydroxocobalamin, Hydrocyanic Acid (HCN), Sodium Cyanide (NaCN) , Potassium Cyanide (KCN), Cytochrome Oxidase.

INTRODUCTION

Cyanide is found in manufacturing and industrial sources such as insecticides, photographic solutions, and jewelry cleaners. (1)

It has been used as a poison in mass homicides and suicides. During World War II, the Nazis used cyanide as an agent of genocide in gas chambers.(2)

Cyanide poisoning may result from a variety of exposures, including structural fires, industrial exposures, medical exposures such as sodium nitroprusside, and certain foods. (3)

In domestic countries, the most common cause of cyanide poisoning is domestic fires. Cyanide also is used in a number of industrial applications such as electroplating injury production, photography, plastics and rubber manufacturing, and pesticides.(4)

Sodium nitroprusside, a medication used to treat a hypertensive emergency, contains five cyanide groups per molecule. Toxic levels of cyanide may be present in patients who receive prolonged infusions of sodium nitroprusside (5)

Cyanide's main effect is by binding to the enzyme cytochrome C oxidase and blocks the mitochondrial transport chain.(6)

Cyanide poisoning produces cellular hypoxia and depletion of ATP leading to metabolic acidosis. (7)

It is rapidly absorbed. The average lethal dose for potassium cyanide is about 250 mg (8)

As very few people survive severe CN poisoning, reports of late neurological sequelae are rare.(9)

CN poisoning in mild degrees is recognized as a cause of permanent neurological disability, ranging from various extrapyramidal syndromes to post-anoxic vegetative states (10)

Most cases develop over many years. Both parkinsonian symptoms and a dystonia syndrome have been observed (11)

Cyanide poisoning also results from exposure to aliphatic nitrile compounds (e.g. acetonitrile) or by dermal absorption /ingestion of cyanide salts and aliphatic nitriles. Its notoriety as a suicidal, homicidal and genocidal agent is well known (12)

Although some natural products such as silk and wool can release cyanide when burned, practically any substance with carbon and nitrogen can release cyanide when burned (13)

Cyanide toxicity should be suspected in smoke inhalation patients with two or more of the signs of neurological dysfunction, such as changes in mental status, loss of consciousness, and seizure activity (14)

Cyanide is a lethal compound because it binds to ferric iron in

cytochrome oxidase a3, thereby inhibiting oxidative phosphorylation, which leads to the depletion of intracellular adenosine triphosphate (ATP)(15)

Cyanide exists in gas, liquid, and solid forms. It can cause human toxicity via multiple routes including inhalation, ingestion, parenteral administration, and dermal or conjunctival contact.(16)

The intoxication occurs via absorption through skin, smoke inhalation, or more rarely, accidental oral intake (17,18)

Of note, mouth-to-mouth resuscitation is contraindicated in cyanide poisoning because of the risk to the provider of CPR (19)

Even individuals who survive may have signs of anoxic encephalopathy. Anecdotal reports indicate that movement disorders and neuropsychiatric symptoms are not uncommon(20)

History

Hydrogen cyanide was discovered by the Swedish chemist Carl Wilhelm Scheele in 1742.It was formed during a reaction of dilute sulfuric acid with potassium ferricyanide, the so-called red blood leach salt.

Signs and symptoms

When inhaled as a gas, its action occurs within seconds.

Massive doses may produce sudden loss of consciousness and prompt death from respiratory arrest. After ingestion, symptoms appear within minutes, during which the victim may perform certain voluntary acts, such as corking, or throwing away the bottle or walking a little distance.

The major organs/systems involved are the GIT, CNS, respiratory and cardiovascular systems.

Gastrointestinal Tract

The features of GIT involvement occur after the ingestion of cyanides and include a burning taste, throat numbness, salivation, frothing at the mouth, nausea, vomiting, and substernal and epigastric pain

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Central Nervous System

The involvement of CNS leads to dizziness, headache, sweating, anxiety, confusion, drowsiness, syncope, opisthotonus, seizures, coma and death.

Respiratory System

Initially, tachypnea and dyspnea develop due to the stimulation of respiratory center and carotid chemo receptors caused by local hypoxia. Bradypnoea, hypopnea and irregular respiration (characteristically, a short inspiration and prolonged expiratory phase), pulmonary oedema, cyanosis and respiratory arrest in the laterstage. A bitter-almond like odour may be detected in the breath

Cardiovascular System

Initially, hypertension along with reflex bradycardia. This is followed by hypotension, tachycardia, arrhythmias, etc. The venous oxygen tension approaches that of arterial oxygen tension and, therefore, the venous blood in the initial stages is bright red. This may be easily demonstrable by examining the fundus for retinal arteries and veins.

Lactic Acidosis

Lactic acidosis develops in the later stages as cyanide inhibits mitochondrial cytochrome oxidase, thereby blocking electron transport and preventing oxygen utilization and oxidative metabolism. Lactic acidosis occurs as a consequence of anaerobic metabolism.

Mechanism of cyanide poisoning

Cyanide has high affinity for metals like cobalt and trivalent iron, sulfur compounds such as sodium thiosulfate which contains a sulfur-to-sulfur bond. It binds to ferric ion (Fe3+) of cytochrome oxidase in the mitochondria and inhibits it. It blocks cellular respiration by blocking reduction of oxygen to water, resulting in cellular hypoxia and depletion of ATP. The end result is lactic acidosis and disruption of vital functions leading to profound shock and a fatal outcome. In the CNS cyanide triggers the release of NMDA which leads to seizures. Patients die of cardio-respiratory arrest secondary to dysfunction of the medullary centres.

It exists in gas, liquid, and solid forms and can cause human toxicity via multiple routes including inhalation, ingestion, parenteral administration, and dermal or conjunctival contact. A blood cyanide concentration of 40 mol/L (approximately) brings in the signs & symptoms of cyanide poisoning. The clinical features are divided into early & late stages. Headache, dizziness, confusion, mydriasis, altered level of consciousness, seizures and coma can be the early signs. Early respiratory and cardiovascular findings include tachypnea and tachycardia, while late findings include apnea, hypotension, and cardiac arrhythmia. Hypotension and bradycardia are common in cyanide poisoning.

Absorption, Fate and Excretion

Liquid HCN can be absorbed through all mucous membranes and skin. The gaseous form is readily absorbed through the respiratory tract. Absorption of HCN is quicker than its salts. Salts(cyanides) may vary in their rate of absorption. The rapidity with which the salts, upon ingestion, cause death will depend upon the amount of hydrochloric acid present in the stomach and the subsequent liberation of hydrogen cyanide on reaction with the acid of the stomach. It has, therefore, been suggested that those who are achlorhydric cannot be poisoned by cyanides. This is doubtful because water in the gastric juice and the tissues of the stomach can hydrolyse cyanide and liberate hydrocyanic acid. Apart from this, food in the stomach delays the conversion of the salts to HCN and further delays the process of absorption. All these account for higher fatal dose and longer fatal period of KCN and NaCN.

After absorption, the greater part is converted by a mitochondrial enzyme, rhodanese, into thiocyanate, which is nontoxic. A small amount is eliminated through the expired air, which is appreciable in the form of bitter almond like smell of the expired air. The main route of excretion is urine. (Cyanide is 60% protein-bound concentrated in red cells, and has a volume of distribution of 1.5 L/kg body weight.)

Diagnosis

The diagnosis is based upon the history and physical examination. Although the measurement of whole-blood cyanide level will confirm the diagnosis, cyanide assays are not routinely available and the decision for the treatment needs be based on clinical finding. Lactate levels have been used as surrogate marker.

(A blood cyanide level of >0.2 µg/ml is considered toxic. Lethal cases have usually had levels above 1 µg/ml.)

Treatment

The treatment regimen consists of stabilization, decontamination and antidote therapy

Stabilization:

It includes assisted ventilation, oxygen administration, cardiac monitoring, treatment of metabolic acidosis, vasopressors for hypotension. (Oxygen at 1 atmosphere is advocated along with nitrite and thiosulphate. The major effect of oxygen appears to be on the rhodanese reaction, although the enzyme itself is not known to be sensitive to oxygen.)

Antidotal Therapy:

It comprises of three steps:

The first step consists of administration of amyl nitrite as a first-aid measure. (One ampoule of 0.2 ml is broken between two pads of gauze and placed over the airway. It is inhaled for 30 seconds of each minute and using a fresh ampoule every 3 minutes.)

The second step consists of giving sodium nitrite (as a 3% solution at a dose of 10–15 ml/300–450 mg slow infusion intravenously over 5–10 minutes). These nitrites induce the formation of methemoglobinemia. The affinity of methaemoglobin for cyanide exceeds that of cytochrome a3, leading to dissociation of the cyanide–cytochrome complex.

The third step involves the administration of sodium thiosulphate (as a 25% solution at a dose of 50 ml/12.5 gm intravenously, 3–5 ml per minute). Thiosulphate serves as a substrate for the enzyme rhodanese, which mediates the conversion of cyanide to the much less toxic thiocyanate, which is excreted in the urine. Although the enzyme rhodanese is widely distributed in the body, liver rhodanese probably plays the major role in cyanide detoxification. It is an endogenous mechanism for cyanide metabolism, but the administration of exogenous sulphur greatly accelerates the rate of reaction (nitrite-thiosulphate therapy can be repeated after an hour, if need arises).

Postmortem appearances

The skin presents a livid or violet appearance. Postmortem staining is often bright red due to formation of cyan-methaemoglobin, and also due to the fact that the tissues cannot take up oxygen of the blood, leaving it bright red even in the veins (cyanide being lethal in small quantities and, therefore, the total amount of the poison in the body may not be sufficient for generalized discolouration). The fingers may be clenched, fingernails blue and there is usually froth at the mouth and nostrils. The eyes may be bright, glistening and prominent with dilated pupils Jaws are usually firmly closed. Rigor mortis sets in early and lasts longer.

Internally

The odour of hydrocyanic acid may be noticed on opening the body, but it is liable to fade quickly. The cranial cavity should be opened first, as the odor is usually well-marked in the brain tissue. Blood-stained froth may be found in the trachea and bronchi. Pulmonary oedema is evident. The mucosa of the stomach and intestines is often congested.

In case of cyanides, lips and mouth may be corroded and the mucous membranes of the stomach and duodenum may be bright red to brown in color due to the effect of potassium carbonate (present as an impurity in the potassium cyanide) and the probable formation of cyanhaemochromogen from the effects of the cyanide on hemoglobin in the presence of an alkali. The brain, lungs and blood, in addition to other viscera, should be preserved for chemical analysis. (Lung should be sent intact sealed in nylon bag. Spleen is said to be the best specimen for cyanide analysis since it generally has the highest concentration of the poison owing to enough presence of RBCs.

Mohan Kumar to Cyanide Mohan: From mild-mannered school teacher to dreaded serial killer

Mohan Kumar, a former primary school teacher from Dakshina Kannada, had admitted to killing at least 20 women between 2004 and 2009 by poisoning them with cyanide. He also confessed to befriending them with the offer of marriage and then stealing their jewellery after killing them (21)

Two die after consuming liquor laced with cyanide in ; two arrested for murder

The two men, who are believed to have consumed liquor was laced with cyanide and they were allegedly poisoned to death over a family feud, police sources said. The police added that Palanigurunathan, 56, a blacksmith of Thathankudi Main Road in Kuthalam taluk, was running a workshop on Manganallur Main Road.(22)

Thanjavur liquor deaths | T.N. police suspect cyanide may have been mixed to kill one of the victims

A forensic analysis of a sample of the leftover liquor confirmed the presence of cyanide, according to sources. A day after two persons died due to suspected cyanide poisoning after consuming liquor at a licensed Tasmac bar in Thanjavur, police sources claimed it could have been a case of murder, targeting 36-year-old cab driver Vivek, one of the victims.

MIC had delayed, recurrent cyanide toxicity, reveals ICMR report on Bhopal gas tragedy

Methyl isocyanate (MIC) which killed thousands of people in Bhopal in December, 1984, following a leak in its pesticide unit, was not highly poisonous, a report released by the Indian Council of Medical Research (ICMR) has established that it caused not only “acute cyanide toxicity” but also “delayed or recurrent cyanide toxicity” due to thermal decomposition of the gas.(23)

it's **'Cyanide Siva': Andhra Pradesh man held for poisoning 10**

Andhra Pradesh police have arrested an alleged serial killer who murdered as many as 10 people in just 20 months. West Godavari SP Navdeep Singh Grewal told reporters that Siva trapped unsuspecting victims by using a variety of tricks

Chicago Tylenol murders

The Chicago Tylenol murders were a series of poisoning deaths resulting from drug tampering in Chicago metropolitan area in 1982. The victims consumed Tylenol branded acetaminophen capsules that had been laced with Potassium cyanide. Seven people died in the original poisonings, and there were several more deaths in subsequent copycat crimes.(24)

CONCLUSION

The virulent cyanide is due to its irrevocable ferric ion complex of cytochrome oxidase in the mitochondrial respiratory chain. This binding blocks oxidative phosphorylation catalyzed by cytochrome oxidase, thus impeding aerobic respiration, which rapidly leads to depletion of ATP, resulting in cell injury or death. Limited data on human poisonings with cyanide salts suggest that hydroxocobalamin is an effective antidote. The outcomes

after cyanide poisoning depend on the concentration. Those with mild exposure and few symptoms usually have a good prognosis, but those with severe exposure usually have a poor outcome.

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